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10/623,864	07/22/2003	Dietrich Wilhelm Schacht	6102-000069/US	6414

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,864	SCHACHT ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/09/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, filed 03/09/09, has been fully considered and made of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 1-13 are currently pending in this application.

Claim 7 is withdrawn.

Claims 1-6 and 8-13 are under examination.

Miscellaneous

It is noted that the rejection statement under 103(a) of the Office action, mailed 11/12/08, page 4, inadvertently omits the citation of Lauterbach. Also, there is a typographical error in the name of this reference in the body of the action. The action is hereby amended to correct the inadvertent errors as shown below. The examiner wishes to thank applicant for pointing out these inadvertent errors.

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, and 8-13 are rejected as being unpatentable over D'Angelo et al. (US Patent 5,932,240), in view of Lauterbach (US Patent Application No. 2003/0027793 A1).

Claim 1 recites "[a] transdermal delivery system (TDS) comprising a backing layer, a self-adhesive matrix containing rotigotine and a protective foil or sheet to be removed prior to use, wherein the self-adhesive matrix comprises a solid or semi-solid semi-

permeable polymer (1) wherein rotigotine in its free base form is incorporated, (2) which comprises a multitude of microreservoirs within the matrix, said microreservoirs containing rotigotine, (3) which is permeable to the free base of rotigotine, (4) which is substantially impermeable to the protonated form of rotigotine, and (5) wherein the microreservoirs have a maximum diameter that is less than the thickness of the matrix; and wherein the backing layer is inert to the components of the matrix." Claim 2 recites "wherein the microreservoirs have a mean diameter in the range of 0.5 to 20 μm." Claim 3 recites "wherein the self-adhesive matrix is free of particles that can absorb salts of rotigotine at the TDS/skin interface." Claim 4 recites "wherein the self-adhesive matrix comprises a silicone pressure sensitive adhesive."

Claim 5 recites "wherein the self-adhesive matrix comprises two or more silicone pressure sensitive adhesives as the main adhesive components." Claim 6 recites "wherein the two or more silicone pressure sensitive adhesives comprise a blend of a high tack silicone pressure sensitive adhesive comprising polysiloxane with a resin and a medium tack silicone pressure sensitive adhesive comprising polysiloxane with a resin." Claim 8 recites,"wherein the microreservoirs additionally contain at least one crystallization inhibitor comprising soluble polyvinylpyrrolidone, a copolymer of polyvinlypyrrolidone and vinyl acetate, polyethylene glycol, polypropylene glycol, glycerol, a fatty acide ester of glycerol and/or a copolymer of ethylene and vinyl acetate." Claim 9 recites "wherein the at least one crystallization inhibitor comprises soluble polyvinylpyrrolidone." Claim 10 recites "comprising within the matrix 10^3 to 10^9 microreservoirs per square cm [sic]…" Claim 11 recites comprising within the matrix

10^6 to 10^9 microreservoirs per square cm [sic]." Claim 12 recites "wherein the microreservoirs have a maximum diameter not greater than 35 μm." Claim 13 recites "wherein the microreservoirs have a maximum diameter of 2.5 to 30 μm."

D'Angelo et al. (US Patent 5,932,240) teach multidose transdermal drug delivery system comprising a laminate composite with a plurality of compartments, wherein each compartment is a reservoir for a unit dose of a drug active to be transdermally administered, wherein said unit doses being in the form of a multiphase composition of microspheres wherein an internal phase comprises the drug actives and adjuvants, and said internal phase is surrounded by an outer phase of film-forming polysaccharides engrafted with transdermal promoters, said microspheres being distributed through a diffusible matrix of said composition (abstract and reference claim 1). The patch assembly consists of a base in which the steady state dosage is contained as needed by the patient and individual medicament reservoirs which may be activated by either a "tear-and-release" or "pull-and-release" mechanism (i.e. backing layer; col. 2, lines 56-61). The reservoirs contain medicament which can be the same as contained in the base or various unit dosages of the base (col. 2, lines 61-67). D'Angelo et al. teach that various drugs can be delivered in unit doses, including antiparkisonism drugs (col.1, lines 57 to col. 2, line 21; col. 2, line 67 to col. 3, line 8). D'Angelo et al. teach a multidose transdermal drug delivery system comprising a laminate composite of a drug-permeable membrane to be placed in contact with a patient's skin; a transfer gel layer disposed on the membrane; a permeable membrane disposed on the transfer gel layer; overlaid impervious drug enclosure means for receiving and protectively enclosing a

drug active to be transdermally administered; wherein the drug enclosure means and the permeable membrane defining a plurality of compartments therebetween defining reservoirs for respective unit doses of the drug active; and individual activation means for releasing unit doses of the drug active form respective ones of the compartments for contacting with the patient's skin (col. 3, lines 9-23). D'Angelo et al. teach reservoirs comprising microencapsulations of the drug active, wherein the drug active may be insulin encapsulated into capsules of substantially 1 to 150 microns diameter, the microencapsulations are formed of a layer of polymer encapsulating the drug active, the polymer layer having drug-penetration moieties engrafted thereon (col. 3, lines 51-57). D'Angleo et al. disclose that laminate composite forming the reservoirs for the drug actives and associated vehicles may be formed from flexible or rigid materials, including regenerated cellulose (cellophane), ABS polymer/cellulose acetate (col. 4, lines 44-56). D'Angelo et al. teach Cotran 9872 acrylate adhesive for adhering the patch to the skin (= **self-adhesive layer**; col. 7, lines 2-9).). D'Angelo et al. teach that useful dimensions for the patch are approximately one inch by two inches and up to about one quarter to half inch in thickness (col. 4, lines 61-63), while the size of each reservoir is determined by the volume of the unit dose to be administered (col. 4, lines 63-67). D'Angelo et al. teach that the drugs and their adjuvants are dissolved, suspended, absorbed or contained in matrices or solutions, wherein useful matrices are gels of bipolymers such as alginates, gelatins, chitin, and **PVP** (col. 5, lines 2-3).

Although D'Angelo et al. al. teach that trandermal drug delivery systems wherein various drugs, such as antiparkinsonism drugs may be included in the microreservoirs,

and acrylate adhesive for adhering the patch to the skin, this reference does not teach the specific instantly claimed compound or silicone pressure adhesives (col. 1, line 57 to col. 2, line 21; and col. 7, line 2 to col. 8, lines 24-55).

Lauterbach et al. (US Patent Application Pub. No. 2003/0027793 A1) teach silicone-based transdermal therapeutic system comprising rotigotine as the active ingredient wherein it was shown that rotigotine free base form in a silicone matrix provided unexpectedly high plasma levels of rotigotine (abstract; para. 0014). Lauterbach et al. teach that said silicone-based transdermal therapeutic system must contain at least one amine resistant silicone compound as the main component, wherein the silicone compound is usually a pressure sensitive adhesive or a mixture thereof and will form a matrix in which the other components of the TTS are embedded e.g. polydimethylsiloxane (PDMS)/resin network (para. 0020). Lauterbach et al. disclose that while acrylate system is able to dissolve more drug than the silicone system, silicone in turn allows for a better release of the drug to skin (para. 0012). Lauterbach et al. teach silicone transdermal system comprising a solubilizer, including polyvinylpyrrolidone, polypropylene glycol, ... (para. 0022). Lauterbach et al. teach that a preferred content of rotigotine per patch is in the range of 0.1 to 2 mg/square cm (para. 0027). Lauterbach et al. exemplifies a transdermal therapeutic system using a combination of silicone-type pressure sensitive adhesives, wherein rotigotine was present in free base solution (346.4 g) in ethanol. Lauterbach et al. teach a polyester release liner (SCOTCHPAK 1022). See para. 0040. Lauterbach et al. teach a backing layer that is inert with respect to the constituents of the matrix, a self-adhesive matrix

layer containing an effective quantity of rotigotine or rotigotine hydrochloride and a protective film which is to be removed before use, wherein the matrix system is composed of non-aqueous polymer adhesive system, based on acrylate or silicone; and wherein said matrix is essentially free of inorganic silicate particles (page 2, para 0011)

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teaching of D'Angelo et al. (US Patent 5,932,240) and Lauterbach et al. (US Patent Application Pub. No. 2003/0027793 A1) by adding rotigotine free base to the microreservoirs component of the transdermal formulation taught by D'Angelo et al. (US Patent 5,932,240) to provide multiple unit doses of rotigotine. One would have been motivated to add rotigotine free base to the transdermal delivery system to provide multiple unit doses of rotigotine because D'Angelo suggest that drugs used to treat Parkinson's disease may be included in the microreservoirs of the transdermal patch. Besides, one would appreciate the desirability of administering multiple unit doses, wherein a given dose of a drug is delivered transdermally in multiple doses instead of a single large dose, as this would allow smaller doses of the drug to be administered to a patient per unit of time, which would result in less dose-related side effects. Further, it would have obvious to a person of skill in the art to add a silicone pressure adhesive as taught by Lauterbach et al. to the adhesive component of the transdermal formulation for additive adhesive effect because Lauterkach et al. suggest that mixtures of pressure sensitive adhesives can be used in transdermal formulations and both Lauterbach et al. and D'Angelo et al. teach transdermal formulations. In view of the fact that the cited art teaches all the instant

claimed limitations, the trandermal drug delivery system encompassed by the prior art is capable of performing the intended function (e.g. substantially impermeable to the protonated form of rotigotine).

It is noted that D'Angelo et al. teach PVP, which overlaps with the instantly claimed crystallization inhibitor (claims 8 and 9). Hence, one would reasonably expect that the size of the microreservoirs containing PVP as taught by the cited art would be similar in size to the instantly claimed microreservoirs (claims 10-13). Besides, D'Angelo et al. teach that the size of the microreservoirs can be manipulated depending on the volume of the dose of drug that is intended to be delivered by the transdermal drug delivery system.

It is the examiner's position that it would have been within the scope of skill and knowledge of an artisan skilled in the art to manipulate the size of the microreservoirs, including the maximum diameter, and the thickness/surface area of the matrix because this is routine in the pharmaceutical art.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments

It is noted that Lauterbach et al. is proper 102(e) art because its effective filing date is March 12, 2002, while the earliest possible filing date of the instant application is July 30, 2002.

In response to applicant's arguments, it is noted that D'Angelo et al. teach microreservoirs having comprising microencapsulations of the drug active having a diameter substantially of 1 to 150 microns, wherein the microencapsulations are formed of a layer having drug-penetration moieties engrafted thereon (col. 3, lines 51-57) such that one would reasonably expect that said microreservoirs would have a maximum diameter that is less than the thickness of the self-adhesive matrix since the self-adhesive matrix provides a means to activate the reservoirs by either a "tear-and release" or "pull and release" mechanism (col. 2, lines 56-63; col. 4, line 27 to col. 5, line 33) which would be expected to be visible to the naked eye. Thus, applicant's argument that Lauterbach teaches away from reducing the size of the microreservoirs relative to the thickness of the patch is not found to be persuasive.

Regarding applicant's argument that D'Angelo do not teach a self-adhesive matrix comprising the reservoirs, it is noted that D'Angelo teach reservoirs of drug, hydrogel through major openings in the layer to be applied to the skin, wherein the openings are covered with a Cotran 9710 acrylate adhseive (col. 7, lines 1-7) and therefore the Cotran 9710 acrylate adhesive defines the matrix containing the drug. Since the Coltran 9719 acrylate adhesive (= self-adesive) is intended to be in contact with the skin and it is part of the matrix containing the drug, the matrix is necessarily self-adhesive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As discussed above, D'Angelo suggest that any drug, including anti-parkinson drugs, can be employed in transdermal delivery systems and therefore one would have expected to attempt to prepare a transdermal delivery system comprising rotigotine since rotigotine is an anti-parkinson drug. Hence, applicant's hindsight argument is not found to be persuasive.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 and 8-13 are rejected on the ground of nonstatutory obviousness-type double (ODP) patenting as being unpatentable over claims 5-16 of copending US Patent Application No. 10/429,283 (Appl. '283), in view of D'Angelo et al. (US Patent 5,932,240).

In particular, reference claim 1 is directed towards a transdermal therapeutic system (TTS) comprising a self-adhesive matrix layer containing (-)-5,6,7,8-tetrahydro-6-[propyl [2-(2-thienyl)ethyl]amino]-1-naphtol, a backing that is inert to the components of the matrix, and a protective film that is to be removed prior to use. Unlike the instant claims, the reference claims are not directed to transdermal drug delivery systems comprising rotigotine in microreservoirs. The above discussion of D'Angelo et al. is incorporated by reference. Despite the difference between the instant claims and the reference claims, it would have been obvious to a person of skill in the art at the time

the invention was made to modify the reference transdermal drug delivery system in order to provide multiple unit doses of rotigotine. One would have been motivated to modify the reference transdermal patch to provide multiple unit doses of rotigotine because it would have been desirable to provide multiple unit doses containing small doses of rotigotine to minimize drug-induced adverse events.

Thus, instant claims 1-6 and 8-13 are deemed obvious variants of the limitations of claims 5-16 of Appl. '283 in view of D'Angelo et al. (US Patent 5,932,240).

Claims 1-6, and 8-13 are also rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending US Patent Application No. 10/627,990 (Appl. '990) claims 1-13, in view of D'Angelo et al. (US Patent 5,932,240) and Lauterbach.

In particular, reference claim 1 is directed towards a transdermal delivery system (TDS) comprising a backing layer, a self-adhesive matrix containing an amine functional drug, and a protective foil or sheet to be removed prior to use, wherein the self-adhesive matrix comprises a solid or semisolid semi-permeable polymer. Unlike the instant claims, the reference claims are not directed to transdermal drug delivery systems comprising rotigotine in microreservoirs. The above discussion of D'Angelo et al. is incorporated by reference. Despite the difference between the instant claims and the reference claims, it would have been obvious to a person of skill in the art at the time the invention was made to use any suitable drug, including rotigotine modify the

reference transdermal drug delivery system in order to increase the duration of maintaining therapeutically effective

Thus, instant claims 1-6 are deemed obvious variants of the limitations of claims 1-13 of Appl. '990, in view of D'Angelo et al. and Lauterbach et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Response to applicant's arguments

In response to applicant's arguments in connection with the rejection based on copending application 10/929,283, the above discussion with respect to applicant's response to arguments in connection with the rejection under 103(a) is incorporated by reference. Thus, applicant's arguments that the reference claims in view of D'Angelo et al. fail to establish a prima facie case of obviousness is not found to be persuasive.

Applicant's statement that the present application has an earlier filing date than the reference application and therefore when issued as a patent will expire before any patent issued from the reference application pursuant to MPEP 804.II.B1 is acknowledged. However, the rejection is maintained because applicant's argument fails to substantially traverse the rejection. Thus, the rejection of record is maintained.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the

automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

26 May 2009
/C. R./ Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611